

### Amendments to the Claims

Claim 1 (Currently amended):        A method for modeling cellular metabolism of an organism, comprising:

constructing a flux balance analysis model utilizing stoichiometric mass balances of metabolic and cellular composition information to identify boundaries for available flux distributions;

applying logic constraints to the flux balance analysis model to thereby tighten the boundaries for the available flux distributions.

Claim 2 (Currently amended):        The method of claim 1 wherein at least a subset of the logic constraints ~~protect~~ are capable of protecting against violation of a kinetic barrier.

Claim 3 (Previously presented):       The method of claim 1 wherein the logic constraints further include a set of connectivity restraints.

Claim 4 (Original):       The method of claim 1 further comprising the step of applying mixed-integer linear programming to solve for a desired metabolic outcome.

Claim 5 (Original):       The method of claim 1 further comprising the step of solving for a desired metabolic outcome.

Claim 6 (Currently amended):        A method for modeling cellular metabolism of an organism that improves upon a flux balance analysis model, comprising:

constructing the flux balance analysis model utilizing stoichiometric mass balances of metabolic and cellular composition information to identify boundaries for available flux distributions; and  
applying a plurality of logic constraints to the flux balance analysis model to thereby tighten the boundaries for the available flux distributions.

Claim 7 (Original): The method of claim 6, further comprising selecting the set of logic constraints to protect against violation a kinetic or regulatory barrier.

Claim 8 (Original): The method of claim 6 wherein the logic constraints are defined by a relationship between changes in reaction fluxes and metabolic concentrations.

Claim 9 (Cancelled).

Claim 10 (Original): The method of claim 6 wherein the logic constraints are represented by binary variables.

Claim 11 (Original): The method of claim 10 wherein a first binary variable represents the presence of a reaction and a second binary variable represents the absence of a reaction.

Claim 12 (Original): The method of claim 6 further comprising applying a computational procedure to identify a minimal set of metabolic reactions.

Claim 13 (Original): The method of claim 12 further comprising selecting a growth rate, and wherein the step of applying a computational procedure is applying a computational procedure to identify the minimal set of metabolic reactions capable of supporting the growth rate.

Claim 14 (Original): The method of claim 6 further comprising the step of applying mixed-integer linear programming to solve for a desired metabolic outcome.

Claim 15 (Previously presented): The method of claim 6 further comprising the step of solving for a desired metabolic outcome.

Claim 16 (Previously presented): The method of claim 15 further comprising engineering the change in an organism based on the desired metabolic outcome.

Claims 17-18 (Cancelled).

Claim 19 (Currently amended): A system for modeling cellular metabolism of an organism, comprising:

a flux balance analysis model utilizing stoichiometric mass balances of the metabolic and cellular composition information to identify boundaries for available flux distributions;

a plurality of logic constraints applied to the flux balance analysis model to tighten the boundaries for available flux distributions, the logic constraints selected from the set consisting of qualitative kinetic information constraints, qualitative regulatory information constraints, and differential DNA microarray experimental data constraints.

Claim 20 (Previously presented): The method of claim 1 wherein the logic constraints further include qualitative regulatory information constraints.

Claim 21 (Currently amended): The method of claim 20 wherein at least a subset of the logic constraints protect against violation of a regulatory barrier.

Claim 22 (Previously presented): The system of claim 1 wherein the logic constraints further include DNA experimental data constraints.

Claim 23 (Previously presented): A method for modeling cellular metabolism of an organism, comprising:  
constructing a flux balance analysis model;  
applying constraints to the flux balance analysis model, wherein the constraints include qualitative regulatory information constraints and differential DNA microarray experimental data constraints.

Claim 24 (Currently Amended): The method of claim 23 wherein the ~~logic~~ constraints include logic constraints to protect against violation of a regulatory barrier.

Claim 25 (Previously presented): The method of claim 23 wherein the constraints further include connectivity restraints.

Claim 26 (Previously presented): The method of claim 23 further comprising applying mixed-integer linear programming to solve for a desired metabolic outcome.

Claim 27 (Previously presented): The method of claim 23 further comprising solving for a desired metabolic outcome.

Claim 28 (Cancelled).

Claim 29 (Previously presented): A method for modeling cellular metabolism of an organism, comprising:

constructing a flux balance analysis model;

applying constraints to the flux balance analysis model, wherein the constraints include differential DNA microarray experimental data constraints.

Claim 30 (Currently amended): A method for modeling cellular metabolism of an organism that improves upon a flux balance analysis model, comprising:

constructing the flux balance analysis model utilizing stoichiometric mass balances of metabolic and cellular composition information to identify boundaries for available flux distributions;

applying a plurality of logic constraints to the flux balance analysis model to tighten the boundaries for available flux distributions; and

applying mixed-integer linear programming to solve for a desired metabolic outcome associated with the organism.

Claim 31 (Previously presented): The method of claim 30 further comprising the step of solving for the desired metabolic outcome.

Claim 32 (Previously presented): The method of claim 31 further comprising engineering a change in the organism based on the desired metabolic outcome.

Claim 33 (New): A method for modeling cellular metabolism of an organism, comprising:  
constructing a flux balance analysis model using stoichiometric mass balances of metabolic and  
cellular composition information to identify stoichiometric boundaries for available flux  
distributions;  
determining logic constraints to apply to the flux balance analysis model to tighten the  
stoichiometric boundaries, the logic constraints based on qualitative relationships  
between changes in reaction fluxes and changes in metabolite concentrations; and  
applying the logic constraints to the flux balance analysis model to thereby tighten the  
stoichiometric boundaries.